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Antidepressant Usage in Haemodialysis Patients: Evidence of Sub-optimal Practice Patterns

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Abstract

Background

Depression is common in patients on haemodialysis and associated with adverse outcomes. Antidepressant use is widespread though evidence of efficacy is limited.

Objectives

To study antidepressant management practices in patients on haemodialysis with reference to NICE guidelines on management of depression in adults with chronic physical health problems.

Design

Prospective, multicentre, longitudinal cohort study with 6-15 month follow-up.

Participants

Patients on haemodialysis established on antidepressant medication.

Measurements

Baseline assessment of mood was undertaken using Beck Depression Inventory (BDI-II). Demographic, clinical, and medication data was also collected. Changes in clinical and life circumstances, and medication during follow-up were recorded. At follow-up, BDI-II was reassessed and diagnostic psychiatric assessment undertaken.

Results

Forty-one patients were studied. General Practitioners were the main prescribers (68%). Ten agents were in use, the commonest being Citalopram (39%). Doses were often sub-optimal. At baseline, 30 patients had high BDI-II scores (≥ 16) and 22 remained high at follow-up. Eleven had BDI-II < 16 at baseline. In five this increased on follow-up to ≥ 16 . Sixteen patients (39%) had no medication review during follow-up, 14 (34%) had a dose review, and 11 (27%) a medication change. On psychiatric assessment at follow-up, eight patients had current major depressive disorder (MDD), seven recurrent, and 20 evidence of past MDD. Six displayed no evidence of ever having MDD.

Conclusions

Antidepressant management in patients on haemodialysis reflected poor drug selection, over-prescription, under-dosing and inadequate follow-up suggesting sub-optimal adherence to NICE guidelines. Most patients had high depression scores at follow-up. Antidepressant use in haemodialysis requires reappraisal.

INTRODUCTION

Depression is common in patients on haemodialysis (HD). Estimates of prevalence varies between 23 - 39% dependent on methods used (Palmer et al., 2013, Watnick et al., 2005). Diagnosis is challenging due to symptom overlap between depression and advanced chronic kidney disease (CKD), particularly fatigue and other somatic complaints (Chilcot et al., 2010). Depression is associated with reduced quality of life and increased mortality and may lead to reduced treatment adherence and self-care behaviour, and greater healthcare resource use (Abdel-Kader et al., 2009, Hedayati et al., 2010, Chilcot et al., 2011, Rosenthal Asher et al., 2012, Weisbord et al., 2014).

Literature review on management of depression in CKD

Management of depression in patients receiving HD is difficult. A recent systematic review, carried out under the auspices of the European Renal Best Practice Group, identified only one small and inconclusive RCT and recommended well-designed RCTs in this setting (Nagler et al., 2012). Since then there have been three RCTs. The ASSertID study was a feasibility RCT of sertraline versus placebo in patients on HD. There was no benefit of sertraline over placebo on depression severity over a six-month period, though there were more withdrawals related to adverse effects in the sertraline group (Friedli et al., 2017). A larger placebo-controlled study of sertraline in CKD patients not on dialysis, also found no benefit of sertraline over placebo on mood, though there were more adverse effects in the sertraline group (Hedayati et al., 2017). In a third study there was a marginal, statistically but not clinically significant benefit on mood of sertraline over cognitive behavioural therapy (CBT), though there was no control group (Mehrotra et al., 2019). On the other hand, benefits of group (Duarte et al., 2009) and chair side (during centre-based HD) CBT have been reported (Cukor et al., 2014). Hence though there is some evidence for the benefits of CBT in this setting, there is no firm evidence for the use of antidepressants, and some evidence for an increased prevalence of adverse effects.

Indeed CKD may increase the risk of adverse events associated with antidepressants. Some drugs or their active metabolites may be excreted by the kidney and therefore retained in patients with CKD. The condition leads to a disturbed internal milieu, which may substantially change the pharmacokinetic and pharmacodynamic properties of the drug

(Gabardi and Abramson, 2005). CKD is also associated with accelerated heart disease (Bansal, 2017) and many antidepressants are potentially cardiotoxic (Assimon et al., 2019). Polypharmacy is rife in patients with CKD especially those on dialysis. This significantly increases the potential for drug interactions (Mason and Bakus, 2010).

In addition to the excess of adverse effects noted above (Friedli et al., 2017, Hedayati et al., 2017), use of antidepressants has also been associated with increased risks of altered mental status, falls, and fractures in older patients receiving HD (Ishida et al., 2019).

Furthermore there is an increased mortality risk in HD patients on those SSRIs with a higher propensity to increase QT interval compared to those with lesser propensity (Assimon et al., 2019), though whether use of antidepressants is associated with an increased risk over that associated with depression itself, is not known.

Notwithstanding all this – a large proportion of patients on HD are on antidepressants, in the US, in excess of 20% (Assimon et al., 2019, Saran et al., 2018). In our recent ASSertID study (Friedli et al., 2017), we found that a significant proportion of the HD cohort (11%) at baseline screening was currently taking antidepressants, and that around 20% had previously used these agents. There are no specific UK guidelines for the treatment of depression in CKD. However NICE guidelines for the management of depression in patients with chronic physical health problems (NICE, 2009) recommend use of antidepressants in this group of patients for those with moderate or severe depression, mild depression that complicates the care of the physical health problem, an initial presentation with subthreshold depressive symptoms (less than 5) present for over 2 years, and subthreshold depressive symptoms or mild depression persisting after other interventions. NICE make other recommendations for the management of patients initiated on antidepressants including the timing of review and the indications for dose escalation and switch to alternative therapy.

To study the natural history of antidepressant medication in patients on HD and ascertain adherence to these guidelines we followed up patients in the ASSertID study, who were on antidepressants at baseline screening (and therefore excluded from the RCT phase of the ASSertID study), some 6-15 months later (Friedli et al., 2017). At follow-up, baseline screening tests were repeated, and a full clinical and psychiatric history was obtained, including a formal diagnostic interview.

MATERIALS AND METHODS

Ethics

Ethical approval was obtained (REC reference number 14/EE/0143). The study was sponsored by East and North Herts NHS Trust. All patients provided appropriate informed consent in keeping with the Helsinki agreement.

Patients.

We selected patients using screening data from the ASSertID study. In ASSertID, 709 unselected HD patients were screened for high depression scores ($\text{BDI-II} \geq 16$) to identify patients suitable for the RCT phase of ASSertID. Being on antidepressants was an exclusion criterion for the RCT phase of ASSertID – which compared the effect of sertraline and placebo on major depression. Hence, though patients on antidepressants were excluded from the ASSertID RCT, they were eligible for the follow-up study, which is the subject of this paper. These patients were approached by the research psychiatrist, asked if they were interested in taking part in the follow-up study, and provided with a participant information sheet. If the patient expressed an interest in participating, a follow-up appointment with the study psychiatrist was arranged, at which written consent was obtained.

Data collection

Baseline data

- Demographics - date of birth, gender, ethnicity, marital status, and social class/education, social support.
- Primary renal disease, date of starting renal replacement therapy, and transplantation history
- Weight, estimated urine output (cupfuls per day)
- Comorbidities including the presence of: heart disease, stroke, amputation of limbs, diabetes, cancer, liver disease, lung disease.
- Past history and treatment of depression or anxiety. Any other involvement with psychology or psychiatry services

- Haemoglobin, urea and electrolytes, serum albumin, calcium and phosphate, and Kt/V.
- Screen for depression symptoms with Beck Depression Inventory-II (BDI-II) (Beck et al., 2000). This is a standard screening tool for depression symptoms usually used to identify people high scores which are suggestive of major depressive disorder prior to consideration of referral for psychiatric evaluation. Because of the overlap of uraemic and depressive symptoms the cut-off score is set higher at ≥ 16 in HD patients than in the general population (Watnick et al., 2005, Chilcot et al., 2008b). Patients also completed the Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al., 2001) for which the validated cut-off score is ≥ 10 (Watnick et al., 2005).

Follow-up data

- Full medical and psychiatric history
- History of psychotropic medications and primary prescriber
- Changes in psychological or psychiatric treatment since screening
- Hospital admissions, change in comorbidities and medication since screening
- Major clinical and social events since screening
- Repeat screening with BDI-II and PHQ-9
- Diagnostic interview including the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) to identify the diagnosis of MDD
- Antidepressant adherence and beliefs using Medication Adherence Rating Scale (MARS) (Thompson et al., 2000) and Beliefs about Medications Questionnaire (BMQ) (Horne and Weinman, 1999)

Statistical analysis

The cohort was characterised in terms of the screening data and the additional data collected on the patients' history, using descriptive statistics. Differences between baseline and follow-up parameters were assessed by the paired t test or Wilcoxon signed rank test as appropriate. Other group differences were assessed by t-tests or Mann-Witney tests as appropriate. Group differences in proportions were assessed by the Chi-squared test. Differences between

multiple groups were assessed using ANOVA or the Kruskal-Wallis as appropriate. Logistic regression analysis was carried out to determine predictors of current depression. The setting in which the antidepressant therapy was commenced (primary care, nephrology, psychiatry), and the degree to which subsequent management was consonant with relevant NICE guidelines was analysed descriptively. Analyses were carried out using SPSS version 23 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.)

RESULTS

Seventy-six patients out of the 709 screened (11%) in the ASSertID study, were taking antidepressants at the time of screening. At the time of follow-up, six had been transplanted, one had been transferred to another renal unit, 12 had died, and two refused consent. We could not follow-up any of the patients at one centre for logistic reasons (Figure 1). The demographic and clinical characteristics of the remaining 41 patients are shown in Table 1. Ten different antidepressant agents were being taken (Table 2), the most common being Citalopram (39%). The primary prescribers of antidepressants were General practitioners (68%) followed by nephrologists (22%), and psychiatrists (10%).

Follow-up data is shown in Table 3. There were no significant differences between baseline and follow-up with respect to patient dry weight, pre- and post-dialysis BP, haemoglobin, albumin, and calcium, phosphate and Kt/V (data not shown). Twenty patients had life events and 19 had clinical events during follow-up. Fourteen had both. There was a significant reduction in BDI-II score over the course of the study (26 (IQR 19) to 21 (IQR 17): $p=0.015$). PHQ-9 score fell but not significantly (12 (IQR 9) to 10.5 (IQR 10): $p=0.091$).

At baseline, 30 patients had a BDI-II score ≥ 16 , indicating high depressive symptoms. Of these, 22 remained with high depressive symptoms at follow-up while eight improved (BDI-II < 16 at follow-up). Those who improved had lower BDI-II scores (23 (IQR 10) vs 31.5 (IQR 14): $p=0.006$) at baseline, lower dialysis vintage (44.2 (IQR 37.6) vs 79.8 (IQR 50) months: $p=0.035$), and fewer were anuric (8% vs 41%: $p=0.04$). Age, gender, ethnicity, marital status, comorbidity, haematological and biochemical profile, and clinical events during follow-up, did not differ. Of the 11 with BDI-II < 16 at baseline, five had increased their BDI-II score to ≥ 16 at follow-up. These tended to be younger, 61 ± 12 vs 68 ± 21 years, of greater dialysis vintage (42.1 (IQR 17.6) vs 29.1 (IQR 21.1)) and with higher baseline BDI-II score (10 (IQR 6) vs 7.5 (IQR 7)), though none of these changes was statistically significant. No differences in comorbid load were apparent, though baseline serum albumin was lower in those who deteriorated (32.6 ± 5.1 v 38.8 ± 1.6 : $p=0.019$) and more patients in this group had experienced clinical events,

including below-knee amputation and stroke during follow-up (80% vs 17%: $p=0.036$). Patients who were married/partnered were also less likely to have high depressive symptoms in relation to BDI-II (17% vs 80%: $p= 0.036$).

There had been no review of antidepressant medication during follow-up in 16 patients (39%). Fourteen (34%) had had a dose review. A change in antidepressant medication had occurred in 11 (27%). Most of these changes were instigated by GPs. A significant proportion of patients were taking agents cautioned against or with no available prescribing information in HD patients or taking doses that might be considered sub-therapeutic.

Twenty-seven of the 41 patients (66%) either deteriorated or failed to improve during follow-up (Table 4). There were no differences between these and others with respect to demographic, clinical, or biochemical parameters, except that they tended to have experienced more clinical events during follow-up (58% vs 29%: $p = 0.079$). They also had significantly higher BDI-II and PHQ-9 scores at baseline screening and significantly lower necessity scores on the BMQ questionnaire (Table 4). There were no differences with respect to BMQ concerns scores and no differences in MARS scores. In logistic regression analysis (Nagelkerke R square = 0.440), the independent predictors of deterioration or failure to improve were dialysis vintage (months) (odds ratio 1.046: $p = 0.012$) and clinical events (odds ratio 7.118: $p = 0.026$). Although two-thirds of patients deteriorated or failed to improve during follow-up, only 11 changes in antidepressant prescription (27%) were made during that time.

Patients underwent formal psychiatric examination at follow-up. Based on the MINI, eight patients had current major depressive disorder (MDD), seven recurrent, 20 had past MDD, and six displayed no evidence of ever having had MDD (Table 5). Though there were differences between the groups with respect to age, gender distribution, comorbidity profile, baseline depression scores, clinical and life events during follow-up the only significant differences related to follow-up BDI-II and PHQ-9 scores, which were higher in those with current or recurrent depression. Presumably the lack of significance in other parameters

relates to the small numbers in each of the groups. All 15 patients with current or recurrent MDD at follow-up were among the 27 whose BDI-II scores deteriorated or did not improve during follow-up (Figure 2). Most of the other 27 patients were found to have evidence of past MDD on psychiatric examination though interestingly 2 patients appeared never to have experienced MDD. A change of prescription during follow-up occurred in only four patients of the 15 patients (27%) with current or recurrent MDD. The six patients in the group in which there was no evidence of present or past MDD were significantly older than all others [median age 76.6 years (IQR 10) vs 64.6 (IQR 24): $p = 0.03$], but there were no other differences.

Discussion

Two-thirds of HD patients who were taking antidepressants at baseline had persistently high or deteriorating depressive symptom scores after a mean follow-up of 14 months. A high proportion of these (56%) had clinical depression as diagnosed by the MINI. In addition 15% of the cohort had no evidence of ever having had MDD over their lifetime according to the MINI, in spite of their being on antidepressants.

In most cases antidepressant treatment was initiated in primary care rather than by nephrologists. There may be a number of reasons. Nephrologists may be more likely to think that depression is 'part of the illness and/or its treatment'. They may also be much more aware of the complexity of this cohort in terms of comorbidity and polypharmacy with its hugely increased potential for adverse drug effects and interactions, making them reluctant to add to the tablet burden. Notwithstanding this, it is also not clear what assessments had been made in primary care prior to initiation. NICE recommends that if “a patient with a chronic physical health problem answers 'yes' to either of the depression identification questions but the practitioner is not competent to perform a mental health assessment, they should refer the patient to an appropriate professional”. However only 10% of patients had therapy initiated by a psychiatrist. MINI examination at follow-up found no evidence of prior depression in 15% of patients, suggesting potential overprescribing. This is particularly relevant given the difficulties of diagnosing depression in the setting of advanced CKD, stemming from the overlap of symptoms directly attributable to kidney failure and those of depression (Chilcot et al., 2008a). The treatment initiation issue also highlights the need for effective communication between the GP and the nephrologist.

In terms of the choice of agent NICE recommends “First prescribe an SSRI in generic form unless there are interactions with other drugs; consider using citalopram or sertraline because they have less propensity for interactions”. We found that 10 different agents were being used in these 41 patients. The commonest (39% of prescriptions) was citalopram which is in line with these recommendations. However recent evidence suggests that SSRIs associated with significant QT interval prolongation, such as citalopram, are associated with

an increased risk of sudden cardiac death in patients on HD compared to those with less propensity for QT prolongation such as sertraline (Assimon et al., 2019). Similar considerations apply to escitalopram (5% of prescriptions) (Assimon et al., 2019). A few patients (5%) were taking tricyclic antidepressants, despite these being contraindicated for patients with heart disease. This may be especially risky in HD patients as heart disease is very common in this population, and is the prime cause of death.

It was also apparent that a high proportion of patients had no review or amendment of their antidepressant prescription during follow-up. NICE recommends that, if there is an inadequate response after 4 weeks treatment with a therapeutic dose of an antidepressant that the level of support should be increased, and that dose increase or switch to another antidepressant should be considered. We do not know the full trajectory of antidepressant medication in these patients, though it does appear that many had inadequate follow-up, may have been receiving sub-therapeutic doses, or both. This raises questions about the safe and effective use of antidepressants in this setting. However, given the lack of evidence of the efficacy of these agents in this setting, and their propensity to increase adverse events, we cannot predict that full adherence to the guidelines would necessarily translate into patient benefit.

A high proportion of patients had high depressive symptoms at follow up and many of these were found to have major depressive disorder. The main factors associated with high depression scores ($\text{BDI-II} \geq 16$) at follow-up were high baseline depression scores, higher dialysis vintage and adverse clinical events during the follow-up period. This suggests that changes in situational/exogenous drivers of depression over the interval of study may have influenced the depression measurements, the responses to medication, and the indications to escalate therapy. Patients with high scores also had lower BMQ necessity scores, suggesting that people who think the medication is necessary may respond better or may adhere better to the treatment recommendations. This though was not significant in multivariate analysis.

We have previously discussed the limited evidence base for antidepressant medication in patients on haemodialysis. Though there is a little more evidence for the efficacy of CBT, the

benefits shown were short term (Duarte et al., 2009, Cukor et al., 2014) and a recent study has suggested a marginal benefit of sertraline over CBT (Mehrotra et al., 2019). We need further research on both pharmacological and non-pharmacological approaches to the treatment of depression in this setting. This should include studies aimed at optimising the use of currently available treatment options as well as the investigation of more novel approaches including multimodal antidepressants, augmentation strategies using atypical antipsychotics (Ceskova and Silhan, 2018) and use of neuromodulation techniques including transcranial magnetic stimulation (Bewernick and Schlaepfer, 2015). To our knowledge there is currently no literature on use of these newer approaches in advanced CKD.

There are a number of limitations to our study which need to be borne in mind in its interpretation. In the general population the average depressive episode lasts about nine to 12 months without treatment, although around 20% run a chronic course of two years or longer. Once established, chronic episodes last an average of five to eight years (Wittchen and Jacobi, 2005). This may be a contributory factor to our finding that many patients' antidepressant status remaining essentially unchanged during follow-up. Another factor may be difficulty stopping these agents due to withdrawal effects which may be intense and prolonged (Davies and Read, 2019, Horowitz and Taylor, 2019). These may mimic aspects of depression and indeed some uraemic symptoms. It may be that withdrawal is particularly difficult in this setting. In addition a significant proportion of patients on HD are elderly, frail, functionally impaired and their prognosis is poor. It is difficult to estimate just how responsive such patients may be to treatment with antidepressants.

In summary, a significant proportion of the HD population takes antidepressant medication. Our findings suggest multiple problems with their use in this setting. Most initiation and management of antidepressant medication was carried out in General Practice mandating effective communication with nephrology services. Multiple types of antidepressants were being used, a number of which may be potentially problematic in this setting. There was evidence of over-prescription – in 15% of patients there was no firm evidence of current or past depression. There was inadequate follow-up reflecting sub-optimal adherence to NICE guidelines. In addition, recent randomised studies have failed to confirm efficacy of these agents in the CKD population whilst demonstrating significant issues with adverse effects.

Furthermore there is some evidence of increased mortality risk with some of these agents. This suggests the need for a major reappraisal of the use of these agents in this setting.

Implications for clinical practice

Management of depression in haemodialysis patients is difficult. Diagnosis is problematic due to the overlap between symptoms of kidney disease and depression. There are doubts too about the efficacy of antidepressant agents in this setting. In addition there is an increased potential for adverse effects and drug interactions when these agents are used in advanced kidney disease. This study also suggests that suboptimal use of these agents in this setting is widespread. Further research would inform renal specific recommendations. In the meantime, there is ample scope to optimise the use of antidepressants in every day clinical practice though whether this would translate into patient benefit is uncertain.

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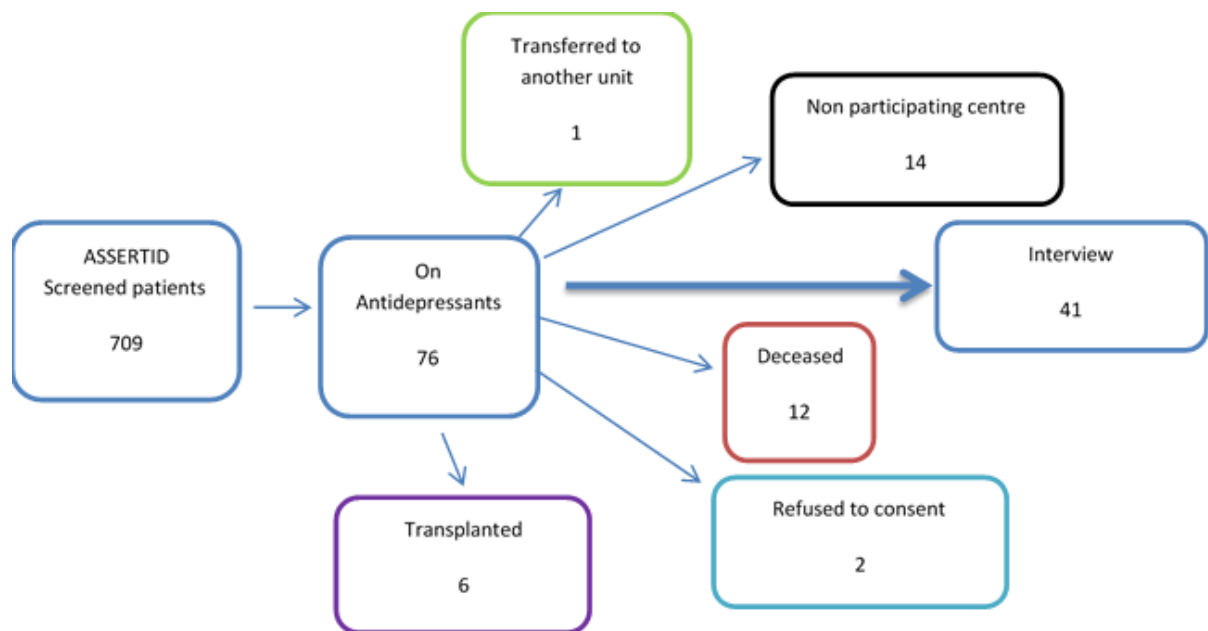


Figure 1. Flow diagram of fate of 709 screened patients over ensuing 6-15 months. Forty-one of the 76 patients on antidepressant medication at screening were available for follow-up studies.

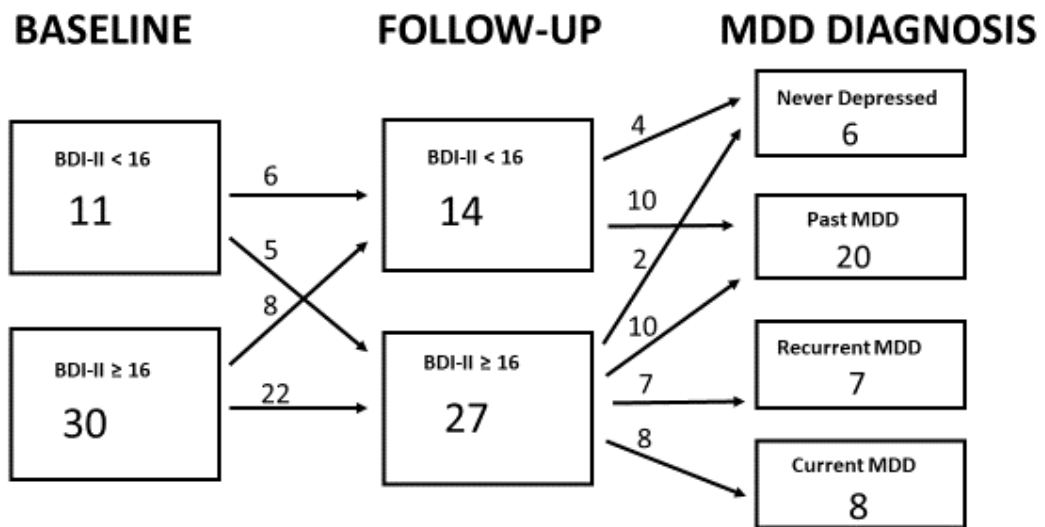


Figure 2. Flow diagram of results of depression symptom screening at baseline and follow-up, together with results of MINI psychiatric examination at follow-up. BDI-II Beck Depression Inventory version 2. MDD major depressive disorder

Age (years)	62 ± 16
Gender (% male)	63
Ethnicity (% white)	73
Married/partner (%)	49
Single (%)	27
Divorced (%)	12
Widowed (%)	12
Diabetes (%)	42
Vintage (IQR) months	42 (56.4)
Heart disease (%)	37
Cancer (%)	22
Amputation (%)	5
Weight (kg)	81 ± 23
Pre-dialysis systolic BP (mmHg)	140 ± 27
Pre-dialysis diastolic BP (mmHg)	75 ± 17
Haemoglobin (g/l)	110 ± 13
Albumin (g/l)	39 ± 4.2
Calcium (mmol/l)	2.26 ± 0.26
Phosphate (mmol/l)	1.50 ± 0.48
Kt/V	1.33 ± 0.31
Previous psychological therapy (%)	32
BDI-II	26 (IQR 19)
PHQ-9	12 (IQR 9)

Table 1. Baseline characteristics of 41 haemodialysis patients on antidepressants. BDI-II Beck Depression Inventory version 2. PHQ-9 Patient Health Questionnaire-9. Kt/V normalised urea clearance per dialysis session. IQR – interquartile range.

Antidepressant	Number of patients	Dose range
Citalopram	16 (39%)	10mg (2), 20mg (10), 30mg (3), 40mg (1)
Fluoxetine	9 (22%)	20mg (8), 40mg (1)
Sertraline	6 (15%)	50mg
Mirtazapine	2 (5%)	30mg
Venlafaxine	2 (5%)	225mg (1), 75mg (1)
Escitalopram	2 (5%)	10mg (1), 15mg (2)
Paroxetine	1 (2%)	10mg
Dothiepin	1 (2%)	100mg
Nortriptyline	1 (2%)	40mg
Duloxetine	1 (2%)	60mg

Table 2. Anti-depressant medication in 41 HD patients at baseline

Mean follow-up (month)	14 ± 5
Primary prescriber	
GP	28 (68%)
Nephrologist	9 (22%)
Psychiatrist	4 (10%)
Medication review	
Antidepressant agents used	10
Dose change	14 (34%)
Medication change	11 (27%)
None	16 (39%)
Events	
Life/social event (%)	20 (49%)
Clinical event (%)	19 (46%)
Depression screening	
BDI-II	21 (IQR 17)
PHQ-9	10.5 (IQR 10)
MINI diagnosis	
Current MDE	8 (20%)
Recurrent MDE	7 (17%)
Past MDE	20 (48%)
No MDE	6 (15%)

Table 3. Follow up data on 41 HD patients on antidepressants at baseline screening. GP general practitioner. MDE major depressive episode. BDI-II Beck Depression Inventory version 2. PHQ-9 Patient Health Questionnaire-9.

	Depressed BDI-II ≥ 16	Non-depressed BDI-II < 16	p-value
Numbers	27	14	
Age (years)	60 \pm 15	67 \pm 18	NS
% Male	56	79	NS
% Married/partner	41	64	NS
% Clinical events	58	29	0.079
% Life events	54	43	NS
% Heart disease	37	36	NS
% Diabetes	44	36	NS
% Cancer	26	14	NS
Dialysis vintage (months)	71.1 (50)	42.2 (37.6)	0.005
BDI-II (baseline)	28 (17)	17 (18)	0.002
PHQ-9 (baseline)	14.5 (7)	7.5 (8)	0.005
BMQ necessity score	12.2 \pm 3	14.5 \pm 2.8	0.022
BMQ concerns score	12.7 \pm 2.8	13.3 \pm 2.5	NS
MARS score	7.9 \pm 1.5	8.6 \pm 1.1	NS

Table 4. Comparison of patients at follow-up whose depression scores were ≥ 16 at baseline screening and deteriorated or failed to improve during follow-up (depressed) and those who remained with BDI-II score < 16 or improved to that level from higher baseline scores (non-depressed). BDI-II Beck Depression Inventory version 2. PHQ-9 Patient Health Questionnaire-9. BMQ Beliefs about Medication Questionnaire. MARS Medication Adherence Rating Scale.

Major Depressive Disorder (MINI Diagnosis)					
	Current	Recurrent	Past	Never	
Number	8	7	20	6	
Baseline					
Age (years)	63 ± 11	58 ± 20	60 ± 17	73 ± 12	NS
% Male	75	43	65	67	NS
% Married/partner	63	29	45	67	NS
% Heart disease	63	29	30	33	NS
% Diabetes	63	57	25	50	NS
% Cancer	38	14	15	33	NS
Dialysis vintage (months)	5.2 (6.2)	5.7 (5.7)	4.3 (4.9)	3.1 (2.2)	NS
BDI-II baseline	32 (17)	18 (16)	26.5 (14)	14.5 (27)	NS
PHQ-9 baseline	12 (6)	9 (10)	12 (9)	7.5 (16)	NS
Follow-up					
% Clinical events	63	71	40	20	NS
% Life events	50	71	40	60	NS
BDI-II – follow-up	28 (13)	27 (12)	16.5 (15)	11 (23)	0.006
PHQ-9 – follow-up	13 (7)	14 (5)	7.5 (6)	6.5 (13)	0.023
BMQ (necessity)	11.4 ± 2.9	13.1 ± 3.1	13.2 ± 2.9	14.2 ± 3.8	NS
BMQ (concerns)	12.1 ± 2.5	12.7 ± 3.6	13.5 ± 2.6	12.3 ± 3.3	NS
MARS (adherence)	8.1 ± 1.5	7.4 ± 1.7	8.5 ± 1.4	8.2 ± 1.0	NS

Table 5. Comparison of baseline and follow-up characteristics based on MINI diagnosis at follow-up. BDI-II Beck Depression Inventory version 2. PHQ-9 Patient Health Questionnaire-9. BMQ Beliefs about Medication Questionnaire. MARS Medication Adherence Rating Scale.